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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,134	07/18/2003	Timothy J. Williams	550-453	2826

23117 7590 09/26/2005

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,134	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-52* is/are pending in the application.

4a) Of the above claim(s) *51 and 52* is/are withdrawn from consideration.

5)☒ Claim(s) *29* is/are allowed.

6)☒ Claim(s) *24-28, 30-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/18/03, 8/11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1-4, 7) on 8/15/05 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-23 have been canceled and new claims 24-52 (8/15/2005) have been added. Claims 51-52 are drawn to methods of using the elected chemoattractant protein. Applicants request rejoinder of the subject matter of the method claims 51-52 (see In re Ochiai (37 USPQ2d 1127 (Fed. Cir. 1995)), in which a new, unobvious material is used in a known process. Ochiai determined that a process was free of the prior art if it employed a product which was free of the prior art. However, only if the product claims of Group I (claims 24-50) are found allowable, the subject matter of Group I will be rejoined with the process claims 51-52 if the process claims are of the same scope as the allowable product claims.

Claims 24-50 are under consideration by the Examiner.

Specification

2. The specification is objected to because of the following:

Page 4, line 26, recites "to attract and/or active eosinophils in vitro" rather than "to attract and/or activate eosinophils in vitro". Appropriate correction is requested.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 30-35, 36-37 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

The claims embrace the naturally occurring product in nature. Therefore, the claims must be limited such that they do not encompass the product in nature. However, since it would that Applicants do not intend to claim a naturally occurring product, amending the claims to recite a recovery and/or purification step will obviate this rejection, i.e. isolated or purified.

Claim Rejections - 35 USC § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 24-27, 30-41, 43-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 24, lines 5-6, for example recites "at least 60% identity with the amino acid sequence of SEQ ID NO:2" which language is new matter in the claim, since the instant specification fails to disclose such a limitation. The specification fails to provide proper support for this language in the claims for the following reason:

The specification page 3, lines 9-14, discloses:

"Other guinea-pig eotaxins will generally have at least 50% overall homology with the sequence shown in SEQ.ID. NO. 1 (Figure 7) at the amino acid level. The homology may be at least 60%, for example at least 70%, for example at least 80% with the sequence set out in SEQ.ID. NO. 1 and in Figure 7."

The specification does not disclose the specific limitation of "at least 60% identity with the amino acid sequence of SEQ ID NO:2" as recited in the claims 24-27, 30, 36, 38-41, 43, 49 and the specific limitation of "at least 80% homology with the amino acid sequence of SEQ ID NO:2" as recited in the claims 31-35, 37, 44-48, 50. This rejection can only be obviated by reciting the specific limitation for which there is support in the instant specification.

4b. Claims 24-28, 30-50, are rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a polypeptide having at least 60%, and 80% amino acid sequence identity with a particular disclosed sequence (SEQ ID NO:2). The claims do not require that the polypeptide possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that are defined only by sequence identity. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity and a function. There is not even identification of any particular portion of the structure that must be conserved for the biological activity of inducing eosinophil accumulation and eosinophil activation *in vitro* and *in vivo*. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics and structure/function relationship, the specification does not provide adequate written description of the claimed genus.

Vas-cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the ad that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the written description' inquiry, whatever is *now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only a polypeptide of amino acid sequence set forth in SEQ ID NO:2 as recited in claim 29, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

4c. Claims 24-28, 30-50, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated protein comprising the amino acid sequence of SEQ ID NO:2 does not reasonably provide enablement for an isolated protein comprising an amino acid sequence having at least 60% identity or homology with the amino acid sequence of SEQ ID NO:2 or an isolated protein comprising an amino acid sequence having at least 80% identity or homology with the amino acid sequence of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 24, for example, is overly broad in its limitation of "at least 60% sequence identity" because no guidance is provided as to which of the myriad of polypeptide molecules encompassed by the claims will retain the characteristics of the desired polypeptide which is capable of at least one of inducing eosinophil accumulation and eosinophil activation in vitro and in vivo. Variants of a nucleic acid can be generated by deletions, insertions, and substitutions of nucleotides, but no actual or prophetic examples on expected performance parameters of any of the possible variants of the claimed nucleic acid molecule or muteins of the protein molecule have been disclosed. Furthermore, it is known in the art that even single amino acid changes or

differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate and use a polypeptide having at least 60% or 80% amino acid sequence identity with SEQ ID NO:2 other than the polypeptide of SEQ ID NO:2 exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of

ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of the claims, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 38-50 are drawn to a polypeptide which is a species homologue of the protein of SEQ ID NO:2. The specification provides only sequence data to allow one to characterize the protein (see page 4, lines 14-22). Many distinct proteins may share the same activity, so that even if one were to determine a biological activity of the protein, say inducing eosinophil accumulation, many distinct proteins would have this activity (e.g. many different cytokines like RANTES and MIP-1α). As a result, if one were to isolate a protein from a different species that had the same activity, one could not reasonably predict if the isolated protein was a species homologue of the original protein because one could not determine if the sequence difference between the original and isolate were due to species differences or to the proteins being non-homologous but sharing the same activity. Even though assays are provided to test for the desired activities (Example 4, pages 24-26), it would be undue experimentation to conduct every assay in the hopes of identifying a specific activity, and no guidance is provided to enable a skilled artisan to predict which activity the protein is likely to have. Further, the specification provides insufficient guidance to allow one to obtain species homologues because the method (pages 12-13) recites only "Screening may be carried out using a probe comprising sequences

characteristic of an eotaxin, in particular, sequences that distinguish the eotaxin from other related cytokines, for example, RANTES and MIP-1α. It may be preferable to use a long probe, for example, a probe comprising a nucleic acid sequence encoding a full-length eotaxin polypeptide."

There is no information about how to identify a "suitable" probe or primer. Additionally species homologues often display low sequence identity so that identification based solely on sequence similarity is impossible. Under such common circumstances, if one cannot test for the expected activity of the encoded putative species homologue, then it is impossible to identify species homologues. For example in The Cytokine Facts Book (1994), Robin Callard and Andy Gearing. Academic Press Inc. San Diego, CA, the amino acid sequence of IL-2 (interleukin-2) from human compared to mouse differs by 16 amino acids in length (page 39, table) and share only about 60% identity (page 39, "Crossreactivity" section). Based solely on sequence, it would be clearly impossible for one skilled in the art to identify the mouse and human proteins as species homologues; however, when one is able to compare a known or putative activity (page 39, "Bioassays" section"), identity can be confirmed.

Furthermore, Reeck et al. (line 1-2) point out, ""Homology" has the precise meaning in biology of "having a common evolutionary origin,"...".

It is stated at the top of column 2 that:

A similarity, then, can become a fully documented, simple fact. On the other hand, a common evolutionary origin must usually remain a hypothesis, supported by a set of arguments that might include sequence or three-dimensional similarity. Not all similarity connotes homology but that can be easily overlooked if similarities are called homologies. Thus, in this third case, we can deceive ourselves into thinking we have proved something substantial (evolutionary homology) when, in actuality, we have merely established a simple fact (a similarity, mislabeled as homology). Homology among similar structures is a hypothesis that may be correct or mistaken, but a similarity itself is a fact, however, it is interpreted.

Reeck et al. provided emphasis to the above reasons for not being able to identify, if one is able to isolate candidates, species homologues as claimed because of the lack of guidance and information in the current specification.

Claim rejections-35 USC § 112, second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27, and 41, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 recites the limitation "one peptide" in line15. There is insufficient antecedent basis for this limitation in the claim.

Claim 41 recites the limitation "one peptide" in line15. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

Claim 29 is allowable.

Claims 24-28, 30-50 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
September 19, 2005